UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,630	06/29/2004	**Allan J. Clarke**	P51216	2988

20462 7590 07/09/2008

SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER	
SASAN, ARADHANA	
ART UNIT	**PAPER NUMBER**
1615	

NOTIFICATION DATE	DELIVERY MODE
07/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/500,630	CLARKE, ALLAN J.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/29/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

Restriction Response

1. Applicant's election without traverse of Group I (claims 1 and 3-41) in the reply filed on 4/24/08 is acknowledged.

2. Claims 2 and 42-50 were cancelled.

3. Claims 1 and 3-41 are included in the prosecution.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 6/29/04 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement.

See attached copy of PTO-1449.

Specification

5. The disclosure is objected to because of the following informalities:

   a. There is a typo on Page 4, line 26; "supermicrocelllar" should be "supermicrocellular".

   b. There is a typo on Page 9, line 11; "it is has" should be "it has".

   c. Page 13, line 6 is missing a period after "nozzle 46".

   d. There is a typo on Page 23, line 11; "pulsitile" should be "pulsatile".

   e. There is a typo on Page 26, line 23; "be adjusting" should be "by adjusting".

f. There is a typo on Page 62, line 4; "in the are" should be "in the art".

g. The use of the following trademarks has been noted in this application: AC-DI-SOL® (Pages 33 and 50), SYLOID® (Page 29), MALTRIN® (Pages 28, 35, 48-56), and KOLLIDON® (Pages 24 and 33). They should be written in all capital letters wherever they appear; or alternatively, they should be denoted with the registered trademark symbol, ®, and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Objections

6. Claims 13 and 31 are objected to because of the following informalities: line 2 of each claim has a typo; "opacifiers" should be "opacifier".

7. Claim 24 is objected to because of the following informalities: line 3 of the claim is missing a comma after polyalditol.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 11, 12, 29 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11 and 29 contain the trademark/trade name AC-DI-SOL® and claims 12 and 30 contain the trademarks/trade names CAB-O-SIL® and SYLOID®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name AC-DI-SOL® is used to identify/describe sodium carboxymethylcellulose, the trademark/trade name CAB-O-SIL® is used to identify/describe fumed silica, the trademark/trade name SYLOID® is used to identify/describe silica and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1, 3-7, 9-25 and 27-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190).

The claimed invention is a pharmaceutical dosage form suitable for oral administration comprising a molded microcellular polymeric material and a pharmaceutically acceptable active agent. The molded microcellular polymeric material is a non-thermosetting polymerized plastics material.

Breitenbach teaches solid, foamed active ingredient preparations based on melt-processable polymers (Col. 1, lines 5-7). Suitable active ingredients include analgesics (acetylsalicylic acid), antibiotics (amoxicillin), antidepressants (fluoxetine) and antihypertensives (verapamil) (Col. 1, line 38 to Col. 2, line 38). Suitable polymers such as melt processable homo- or copolymers of N-vinylpyrrolidone or mixtures of such polymers are disclosed (Col. 2, lines 58-60). "The active ingredient preparations may furthermore also comprise starches ..." (Col. 3, lines 21-22). Conventional pharmaceutical ancillary substances such as bulking agents (mannitol, sorbitol, xylitol), lubricants (stearates of aluminum or calcium), plasticizers (polyethylene glycol), dyes and stabilizers that can be included in the preparation are also disclosed (Col. 3, lines 26-60). "The degree of foaming of the active ingredient preparation can be controlled by the amount of blowing agent added and the extrusion temperature. A high degree of foaming results in a lower density and thus a high rate of dissolution of the active ingredient form" (Col. 4, lines 61-65). "The foamed active ingredient preparation is

subsequently shaped to the required active ingredient forms … by pelleting, granulating or tableting by known processes" (Col. 5, lines 2-5).

Breitenbach does not expressly teach a molded microcellular dosage form.

Jane teaches "… a biodegradable, soy protein-based thermoplastic composition. The composition is made of soy protein combined with a foaming agent, an organic plasticizing agent, and an aqueous medium such as water, and additives as desired. Articles formed from the composition have a foamed, cellular structure, and are biodegradable and possess a high degree of tensile strength, low density, and water resistance." (Col. 1, lines 42-51). "The composition is composed of about 100 parts soy protein that is preferably soy protein isolate, … and about 0.1-10 parts of a foaming agent, … about 5-60 parts of an organic plasticizing agent that is preferably glycerol, ethylene glycol or propylene glycol, and about 5-50 parts aqueous medium which is preferably water. One or more additives such as a filler, lubricant, colorant, preservative, and bleaching/whitening agent, can be included as desired" (Col. 1, lines 54-65). "The mixture can be molded into an article by compression molding" (Col. 2, lines 3-4). "Advantages of the protein based thermoplastics include excellent biodegradability, water resistance, and a low cost production" (Col. 2, lines 11-24). Polyethylene glycol is disclosed as a plasticizer, along with mannitol and maltitol (Col. 3, lines 51-64). Starches including corn or wheat starch can be used as fillers (Col. 4, lines 36-44). "Natural and modified gums such as xanthan gum, guar gum, locust bean gum, gum arabic, alginates, carrageenan, pectin, agar, konjac flour, and the like, can also be included as a filler in the composition" (Col. 4, lines 54-57). Cellulose derivatives such

as methylcellulose, carboxymethylcellulose, hydroxymethylcellulose, hydroxypropylcellulose and sodium carboxymethylcellulose can also be used as fillers (Col. 4, lines 58-62). Lubricants and colorants are disclosed (Col. 5, lines 11-35). Examples disclose molded articles with a foamed appearance and a closed cell structure with an average cell diameter of about 50μm (Col. 8, lines 12-14).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a solid, foamed active ingredient preparation, as taught by Breitenbach, combine it with the foamed microcellular composition, as taught by Jane, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Jane teaches that the foamed microcellular composition has the advantages of excellent biodegradability, water resistance, and a low cost production" (Col. 2, lines 11-24).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of a pharmaceutical dosage form would have been obvious over the solid, foamed active ingredient preparation that can subsequently be shaped by pelleting, granulating or tableting by known processes, as

taught by Breitenbach (Col. 1, lines 5-7 and Col. 5, lines 2-5). The limitation of a molded microcellular polymeric material and a non-thermosetting polymerized plastics material would have been obvious over the melt processable homo- or copolymers of N-vinylpyrrolidone, starches, mannitol, sorbitol and xylitol as taught by Breitenbach (Col. 2, lines 58-60, Col. 3, lines 21-22 and Col. 3, lines 33-35). The limitation of the molded polymeric material would have been obvious over the molding of the mixture as taught by Jane (Col. 2, lines 3-4). The limitation of a pharmaceutically acceptable active agent would have been obvious over the active ingredients include analgesics (acetylsalicylic acid), antibiotics (amoxicillin), antidepressants (fluoxetine) and antihypertensives (verapamil), as taught by Breitenbach (Col. 1, line 38 to Col. 2, line 38).

Regarding instant claims 3-6, 18-19, 22-24 and 36, the limitation of the non-thermosetting polymerized plastics material that contains at least one polyol and at least one non-thermosetting modifier would have been obvious over the polyols mannitol, sorbitol and xylitol and the starches, as taught by Breitenbach (Col. 3, lines 21-22 and Col. 3, lines 33-35).

Regarding instant claims 7 and 25, the limitation of the starch would have been obvious over the starches taught by Breitenbach (Col. 3, lines 21-22) and over the corn starch, wheat starch, rice starch and potato starch taught by Jane (Col. 4, lines 36-44).

Regarding instant claims 9 and 27, the limitation of the non-thermosetting polymer would have been obvious over the cellulose derivatives such as methylcellulose, carboxymethylcellulose, hydroxymethylcellulose,

hydroxypropylcellulose and sodium carboxymethylcellulose taught by Jane (Col. 4, lines 58-62).

Regarding instant claims 10 and 28, the limitation of a dosage form further comprising a sweetener, a disintegrant, a binder, a lubricant or an opacifier would have been obvious over the lubricants (stearates of aluminum or calcium) taught by Breitenbach (Col. 3, lines 26-60) and the additives such as lubricants and colorants as taught by Jane (Col. 5, lines 11-35).

Regarding instant claims 11 and 29, the limitation of the disintegrant would have been obvious over the sodium carboxymethylcellulose taught by Jane (Col. 4, lines 58-62) and the guar gum, locust bean gum, and agar as taught by Jane (Col. 4, lines 54-57).

Regarding instant claims 12 and 30, the lubricant would have been obvious over the talc, as taught by Breitenbach (Col. 3, line 53).

Regarding instant claims 13 and 31, the opacifier would have been obvious over the calcium carbonate used as a bleaching/whitening agent, as taught by Jane (Col. 5, lines 5-7).

Regarding instant claims 14 and 32, the pharmaceutically acceptable active agent would have been obvious over the active ingredients include analgesics (acetylsalicylic acid), antibiotics (amoxicillin), antidepressants (fluoxetine) and antihypertensives (verapamil), as taught by Breitenbach (Col. 1, line 38 to Col. 2, line 38).

Regarding instant claims 15-17 and 33-35, the limitation of a thermoplastic polymer as the molded microcellular polymeric material would have been obvious over the hydroxypropylcellulose taught by Jane (Col. 4, lines 58-62).

Regarding instant claims 20 and 37, the limitation of the microcellular polymeric material that is a closed cell foam would have been obvious over the closed cell structure as taught by Jane (Col. 8, lines 12-14).

Regarding instant claim 21, the limitation of a rigid microcellular foam would have been obvious over the solid, foamed active ingredient preparation as taught by Breitenbach (Col. 1, lines 5-7 and Col. 5, lines 2-5) and by the closed cell structure as taught by Jane (Col. 8, lines 12-14). The limitation of a solid excipient having voids with a maximum void dimension in the range from about 2 to 100 microns would have been obvious over the closed cell structure with an average cell diameter of about 50μm, as taught by Jane (Col. 8, lines 12-14). The limitation of a void fraction in the range of about 5 to 95 percent would have been obvious over the solid foamed active ingredient preparations taught by Breitenbach (Col. 1, lines 5-7) because Breitenbach teaches that "the degree of foaming of the active ingredient preparation can be controlled by the amount of blowing agent added and the extrusion temperature. A high degree of foaming results in a lower density and thus a high rate of dissolution of the active ingredient form" (Col. 4, lines 61-65). One with ordinary skill in the art would modify the process parameters by varying the amount of blowing agent and the extrusion temperature and achieve the desired void fraction. The recited void fraction range would have been an obvious variant unless there is evidence of criticality or unexpected

results. The limitation of the solid excipient comprising a thermosetting polymerized plastic material and an active pharmaceutical agent combined in a homogenous solid mixture would have been obvious over the solid foamed active ingredient preparations taught by Breitenbach (Col. 1, lines 5-7).

Regarding instant claim 38, the limitation of the homogenous solid mixture that has a sufficiently high solubility in saliva would have been obvious over the "solid, foamed active ingredient preparations ... which comprise the active ingredient homogenously dispersed in the polymeric matrix, dissolve very rapidly and thus permit rapid release of the active ingredient", as taught by Breitenbach (Col. 6, lines 18-22).

Regarding instant claim 39, the voids that are in the form of closed cells would have been obvious over the closed cell structure taught by Jane (Col. 8, lines 12-14).

Regarding instant claim 40, the limitation of the rigid microcellular foam that is enclosed within a skin would have been obvious over the "closed active ingredient forms, i.e., forms in which the layer comprising active ingredient is completely enveloped by a layer without active ingredient" as taught by Breitenbach (Col. 5, lines 9-60). Breitenbach teaches the "production of multilayer partially or completely foamed forms comprising active ingredients by coextrusion. This entails at least two compositions ... at least one of which comprises an active ingredient and at least one of which is impregnated ..." (Col. 5, lines 9-15). One with ordinary skill in the art would find it obvious to completely impregnate the active ingredient layer with another active ingredient layer during the process of routine experimentation.

Regarding instant claim 41, the limitation of the overall density of the dosage form that is substantially less than that of stomach fluids, whereby the dosage form is gastro-retentive would have been obvious because Breitenbach teaches that "the degree of foaming of the active ingredient preparation can be controlled by the amount of blowing agent added and the extrusion temperature. A high degree of foaming results in a lower density and thus a high rate of dissolution of the active ingredient form" (Col. 4, lines 61-65). One with ordinary skill in the art would modify the density of the dosage form with respect to the density of stomach fluids during the process of routine experimentation in order to make the dosage form gastro-retentive.

12. Claims 8 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190) and De Bock et al. (US 5,428,150).

The teachings of Breitenbach and Jane are stated above.

Breitenbach and Jane do not expressly teach a maltodextrin as a non-thermosetting modifier.

De Bock teaches "a process for the extrusion of a starch-containing composition to produce a material suitable for the production of moulded articles in which the composition contains in addition to the starch a starch degradation product selected from starch hydrolysis products having DE's of 1 to 40, particularly a maltodextrin ..." (Abstract). "The hydrolysis products used in the process ... are preferably maltodextrins and more preferably have DE values of 2 to 20" (Col. 3, lines 50-52).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a solid, foamed active ingredient preparation, as taught by Breitenbach, combine it with the foamed microcellular composition, as taught by Jane, further combine it with the maltodextrins, as taught by De Bock, and produce the instant invention.

One of ordinary skill in the art would do this because De Bock teaches that maltodextrins are degradation products of starch and the lower the DE value of the maltodextrin the less the extent of starch degradation (Col. 3, lines 36-47). One with ordinary skill in the art would find it obvious to try maltodextrin in the solid, foamed active ingredient preparation and the starches taught by Breitenbach (Col. 3, lines 21-22) and in the foamed microcellular composition with the corn starch, wheat starch, rice starch and potato starch taught by Jane (Col. 4, lines 36-44) with a reasonable expectation of success of producing a functional molded microcellular polymeric dosage form.

Regarding instant claims 8 and 26, the limitation of the non-thermosetting modifier that is a maltodextrin would have been obvious over the maltodextrins and starches taught by De Bock (Abstract and Col. 3, lines 50-52) and over the starches taught by Breitenbach (Col. 3, lines 21-22) and Jane (Col. 4, lines 36-44).

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-

9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/ /MP WOODWARD/

Examiner, Art Unit 1615 Supervisory Patent Examiner, Art Unit 1615